

**Amendments to the Specification:**

On page 19, please replace the paragraph starting on line 14 and ending on page 20, line 14, with the following:

FIGURES 5A-5C. Macrophage infiltration into hypoxic areas in tumour spheroids (i.e. an in vitro model of tumour hypoxia).

[[i)] FIGURE 5A shows the oxygen profile across a tumour cell spheroid. All but the cells in the outer 100  $\mu\text{m}$  of these 3-D cultures are hypoxic (i.e. experiencing oxygen levels of 0-15  $\text{pO}_2$  mmHg; a level equivalent to that present in hypoxic/necrotic sites in human tumours). This hypoxia is produced by the inability of oxygen to diffuse into the central areas of spheroid. The glucose profile of the spheroid is similar to that seen for oxygen.

[[ii)] FIGURE 5B shows two different tumour spheroids (made of the breast cancer cell line, MCF-7) following co-culture for 24h with the monocytic cell line, U937. The U937 cells (darkly stained cells labelled with a monoclonal antibody to the pan-macrophage marker, CD68) accumulate in the hypoxic rim of viable, but hypoxic tumour cells around the central areas of necrosis ("N").

[[iii)] FIGURE 5C shows the infiltration into tumour spheroids of U937 cells preloaded with fluorescent dye. The top panel is a light micrograph showing the opaque central area of necrosis ("N") which forms in these spheroids as a consequence of nutrient (e.g. oxygen, glucose etc) deprivation. The bottom panel is the same spheroid a fluorescent microscope to show the presence within the spheroid of the fluorescent (i.e. light coloured cells) U937 cells. The latter take up a similar

position to that seen in [(ii)] FIGURE 5B, i.e. they congregate in a collar of hypoxic tumour cells around the central areas of necrosis.